REMARKS

In the instant Action, claims 18-44 are listed as pending and claims 18-44 are listed as subject to restriction and/or election requirement.

Initially, it is noted that the Examiner vacated the previous restriction requirement and issued a new restriction requirement, citing a substantial search burden with the present Application. In the new restriction requirement, the Examiner requires "an election of a single modified somatostatin peptide antagonist as the invention (NOT species) – as each of these modified peptide are deemed distinct", "unless and until Applicant establishes on the written record a substantial, contiguous, core structure, bearing modification, which Applicant himself has searched or is confident is novel".

Of the seven inventions identified by the Examiner at pages of 3-4 of the instant Action, Applicants elect Group I directed to "Claims 18-31 and 44, drawn to formulas directed to distinct somatostatin antagonists, said formulas bearing no substantial core structure; classified in class 514, subclass 2." The remaining Groups II to VII are drawn to various processes for using the product as claimed in the present Application, and Applicants request, in the event that the Examiner finds that any of claims 18-31 and 44 are patentable, the rejoinder of withdrawn process claims.

At page 6 of the instant Action, the Examiner states:

> ... Thus an individual sequence and/or structure search is required of each and every potential oligopeptide from the innumerable number thereto. Therefore, irrespective of which of Group I-VII is the elected invention, Applicant is required elect a single oligopeptide to which the invention (group) will be examined on the merits as drawn to (unless the claims be amended in line with the suggestion outlined at the outset, and the written record clarified to guide the Examiner to a core structure which would allow a coextensive search of said formula compounds without an undue burden). **This requirement is not to be taken as an election of species, but rather an**

election of a single invention, since each compound is assumed to be a patentably distinct invention, in the absence of evidence to the contrary. (emphasis original)

As such, according to the Examiner's statements as quoted above, the new requirement to elect a single oligopeptide as the invention (NOT species) is not required ***if*** the Applicants amend the claims in line with the suggestion outlined at pages 2-3 of the instant Action. Specifically, the Examiner suggests that Applicants amend the formulas of claims 18 and 23 to be "A1-A2-A3-D-Trp-Lys-Thr(Bzl)-Cys-A8-R3, wherein A1-3 are as defined in claim 23, which the Office may coextensively search with X variables at the A loci (A1-A3 and A8)." The Examiner goes on to state, "However, should art be found on the core, and be a somatostatin antagonist, said art will be applied, where the other limitations at the X residues are either taught or obvious variations thereof."

Initially, Applicants find it difficult to accept the Examiner's choices (*i.e.*, either accept the Examiner's suggestion to amend the claims to have 4 fixed amino acids to constitute a "substantial, contiguous, core structure", or elect a single oligopeptide as the invention).

With respect to the first choice, the new requirement to elect a single oligopeptide as the invention (NOT species) is in contrast to the previous restriction requirement (mailed 09/22/2006 by different Examiner, Nancy L. Zhang) wherein Examiner Zhang required Applicants to elect a single disclosed species with respect to a compound as defined in claim 18, and also with respect to a compound as defined in claim 23, under 35 U.S.C. §121, for prosecution on the merits to which the claims shall be restricted if no generic claims is held to be allowable. Examiner Zhang in the previous restriction requirement noted that "Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or

otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141." That is, under 37 CFR 1.141, an allowed generic claim may link a ***reasonable number*** of species embraced thereby. This practice is stated in 37 CFR 1.146 as follows:

> In the first action on an application containing a generic claim to a generic invention (genus) and claims to more than one patentably distinct species embraced thereby, the examiner may require the applicant in the reply to that action to elect a species of his or her invention to which his or her claim will be restricted if no claim to the genus is found to be allowable. However, if such application contains claims directed to more than a reasonable number of species, the examiner may require restriction of the claims to not more than a reasonable number of species before taking further action in the application.

As such, the Examiner's *new* requirement to elect a single oligopeptide as the invention (NOT species) is not sanctioned by 35 U.S.C. §121, nor by 37 C.F.R. §§ 1.141 & 1.146, nor by MPEP §809.02(a). In addition, Applicants respectfully assert that, as a general matter, placing restrictions on the number of species that an applicant can pursue in a single application would have disastrous consequences relative to filing practices by filers who might incorrectly anticipate species they may believe initially are most important versus all that they should have a right to claim and might later be determined to be important, *i.e.*, thousands of compounds made in the course of one's research efforts should be patentable and capable of being protected without one having to pay extra for the particular number of species. In fact, there appears to be no legal basis to charge for species, or restriction of their number, because the case usually is such that a patentable genus is finally determined, covering all species therein, and not a select few.

With respect to the second choice, Applicants' undersigned attorney carefully considered the Examiner's suggestion to amend the formulas of claims 18 and 23 to be be "A1-A2-A3-D-

Trp-Lys-Thr(Bzl)-Cys-A8-R3, wherein A1-3 are as defined in claim 23", to ease the Examiner's search burden. During a telephone conversation (*i.e.*, telephone interview) between the Examiner Audet and Applicants' undersigned attorney, which took place on October 23, 2007, Applicants' attorney pointed out that *none* of the specific compounds listed in claims 22 and 27 have "Thr(Bzl)" as A6. As such, if Applicants adopt the Examiner's suggestion to avoid the new requirement to elect a single oligopeptide as the invention (NOT species), *all* of the specifically claimed compounds of claims 22 and 27 will have to be canceled from the present Application. Having noted that, Applicants' attorney noted for the Examiner that many of the specific compounds of claims 22 and 27 have "Val" as A6, and inquired as to whether the Examiner would be amenable to revise the "substantial, contiguous, core structure" to be "D-Trp-Lys-Val-Cys". The Examiner indicated that that would be acceptable to him. The telephone interview was concluded with the understanding that Applicants' attorney will discuss with Applicants and respond in writing. Applicants' attorney subsequently learned that this core structure is taught in U.S. Patent No. 5,462,926, at Col. 19, line 29, as "H_2-D-Nal-D-Cys-Tyr-**D-Trp-Lys-Val-Cys**-Nal-NH_2". (emphasis added) As such, if Applicants amend the formulas of claims 18 and 23 to be "A1-A2-A3-D-Trp-Lys-Val-Cys-A8-R3" – to avoid having to comply with the restriction requirement to elect a single oligopeptide as the invention (NOT species) – then, as stated in the instant Action, and as quoted above, U.S. Patent No. 5,462,926 is citable to teach this "substantial, contiguous, core structure" "where the other limitations at the X residues are either taught or obvious variations thereof."

Furthermore, Applicants do not understand why the Examiner is insisting upon a ***contiguous*** core structure constituting "at least 50% of said structure (e.g., 4 fixed amino acids)"

in order to ease his search burden. For example, Bass *et al.* (already of record), in the Summary section, states "The antagonists contain a core structure of a DL-cysteine pair at positions 2 and 7 of the peptides." It is clear from the Bass article that those skilled in the art does not consider that it is essential to have a "contiguous core structure constituting at least 50% of said structure" in order to define a "substantial core structure." In fact, claim 18 of the present Application has 4 fixed amino acids as follows "A1-D-Cys-A3-D-Trp-Lys-A6-Cys-A8." According to the Examiner, despite the fact that this sequence has 4 fixed amino acids, it does not define a "core structure" because the 4 fixed amino acids are not "contiguous." Applicants respectfully submit that the Examiner's requirement to amend the formulas of claims 18 and 23 to have a *contiguous* core structure of 4 fixed amino acids in order – in order to avoid having to comply with the restriction requirement to elect a single oligopeptide as the invention (NOT species) – is arbitrary and capricious, and not sanctioned by 35 U.S.C. §121, nor by 37 C.F.R. §§ 1.141 & 1.146, nor by MPEP §809.02(a).

Furthermore, Applicants previously amended claim 18 in response to substantive Office Action,[1] to require that R_3 and the carbonyl group of A8 be reduced together to form H and lower alkyl or a hydroxyl lower alkyl. Specific embodiments demonstrating this requirement are the compounds of claim 22 all of which terminate in either (2R, 3R-(2-hydroxymethyl)-3-hydroxy)propylamide or 2R-(2-naphthyl)ethylamide. As a result of this amendment, A8 can no longer be an amino acid, having lost the required carboxyl group. As such, the compounds of claim 18 are now heptapeptides terminating in H, lower alkyl or hydroxyl lower alkyl. In addition, the previously presented claim 44 is a *subgenus* of claim 18 wherein A8 is a particular

[1] The date of amendment is 04/18/2006, and the date of the substantive Office Action is 10/19/2005.

amino acid, *i.e.*, either Thr or β-Nal, and the carboxyl group of said amino acid has been reduced with the R_3 group to produce either a (2R, 3R-(2-hydroxymethyl)-3-hydroxy)propylamide or 2R-(2-naphthyl)ethylamide moiety at the C-terminal, respectively. Applicants respectfully submit that having 4 fixed amino acids in a **heptapeptide** which has either a (2R, 3R-(2-hydroxymethyl)-3-hydroxy)propylamide or 2R-(2-naphthyl)ethylamide moiety at the C-terminal, is sufficient core structure to significantly ease the Examiner's search burden. Furthermore, the fact that all of the claimed compounds are somatostatin antagonists provides further common feature of the invention to facilitate the Examiner's search.

With respect to claim 23, Applicants previously amended this claim to restrict A2 to a D-aromatic amino acid. This amendment is consistent with the preferred embodiments listed in claim 27 all of which have either D-Phe or D-Cpa in the 2nd position. Both D-Phe and D-Cpa have a benzyl group as part of their side chains. This restriction produces linear octapeptides. In the subsequent Office Action mailed 09/22/2006, Examiner Zhang concluded that "Applicants' argument that the '934 patent (US Patent 5,846,934, already of record) does not disclose a linear octapeptide are found persuasive."

As such, after having complied with previous restrictions requirements and having overcome all cited prior art to secure Notice of Allowance, which was withdrawn, and the new restriction requirement applied by the present Examiner, Applicants are at a loss as to how to comply with this new restriction requirement. Nonetheless, in an effort solely to advance prosecution of this application, Applicants elect, with traverse for the foregoing reasons, the species of the formula **H_2-ß-Nal-D-Cys-Tyr-D-Trp-Lys-Val-Cys-(2R,3R-(2-hydroxymethyl)-3-hydroxy)propylamide**, which is the first compound listed in claim 22. Said compound is

encompassed by claims 18, 19, 22, 33, 34-37, and 44. As noted above, Applicants respectfully but strongly object the Examiner's new requirement to elect a single oligopeptide as the invention (NOT species). As further illustration, the second compound listed in claim 22, **(H)(CH_3CO)-ß-Nal-D-Cys-Tyr-D-Trp-Lys-Val-Cys-(2R,3R-(2-hydroxymethyl)-3-hydroxy)propylamide**, is ***identical*** to the first compound listed in claim 22 in every respect except with respect to R_2. Yet, the Examiner's new restriction requirement would only allow examination of the fist compound of claim 22, and not the second compound of claim 22, even though it is clear that there can be no undue search burden to search these two almost identical compounds together. Should the Examiner decide to maintain the finality of the new restriction requirement, Applicants hereby request that the Examiner provide legal basis for requiring Applicants to elect a single oligopeptide as the invention (NOT species).

Examiner Audet is invited to telephone Applicants' undersigned attorney at (508) 478-0144 to facilitate prosecution of this application.

Applicants hereby authorize the Commissioner to charge any fees that may be due or to credit any overpayment to Deposit Account No. 50-0590.

Respectfully submitted,

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